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Yu Jin, MD, PhD Lutgarde Thijs, MSc Alexandre Persu, PhD Sverre Kjeldsen, MD
Jan A. Staessen, MD, PhD

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Letter to the Editor: No Support for Renal Denervation in a Meta-Analysis

Yu Jin, MD, PhD, Lutgarde Thijs, MSc, Alexandre Persu, PhD, Sverre Kjeldsen, MD, Jan A. Staessen, MD, PhD

Research Unit Hypertension and Cardiovascular Epidemiology, KU Leuven Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium (Y.J., L.T., J.A.S.); Department of Epidemiology, Maastricht University, Maastricht, The Netherlands (J.A.S.); Institut de Recherche Expérimentale et Clinique and Division of Cardiology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium (A.P.); Department of Cardiology, Ullevål University Hospital, University of Oslo, Oslo, Norway (S.E.K.).

Correspondence to:
Jan A. Staessen,
Studies Coordinating Centre,
Research Unit Hypertension and Cardiovascular Epidemiology,
KU Leuven Department of Cardiovascular Sciences,
University of Leuven, Campus Sint Rafaël,
Kapucijnenvoer 35, block D,
Box 7001, BE 3000
Leuven, Belgium.
E-mail: jan.staessen@med.kuleuven.be or ja.staessen@maastrichtuniversity.nl

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We read with interest the recent meta-analysis by Davis *et al* (1) on the blood pressure (BP) lowering effects of renal denervation (RDN) in treatment-resistant hypertensive patients. The authors computed pooled statistics for 3 so-called controlled studies and 9 observational studies. They concluded that the 6-month reductions in systolic/diastolic BP in response to RDN averaged 28.9/11.0 mmHg and 25.0/10.0 mmHg in the controlled and observational studies, respectively. A number of issues need clarification.

First, Dr. Davis used the term controlled to group 2 randomized trials (2,3) and one observational study (4). It is questionable whether truly randomized trials and a nonrandomized study can be combined into a single group. Moreover, one of the randomized studies was of low quality (2). Sample size and primary and secondary endpoints changed across successive design protocols posted at http://www.clinicaltrials.gov up to 1 year after the paper was published (2). We feel that this study (2) should have been excluded based on CONSORT quality standards (5). Furthermore, the spread of the BP responses was not reported for the control group in SYMPLICITY HTN-1(4). In Dr. Davis' Figure 2, the numerical data for the 6-month systolic responses are switched between 2 studies. Moreover, there is discordance between the SDs reported in Dr. Davis' Figure 2 (systolic/diastolic responses at 6 months SD, 9.8/6.0) and the spread of the BP responses in Figure 5 (4.8/3.0 at 6 months) and in the text (5.0/2.0 mmHg at 12 months) of Pokushalov's article. Without clarification, these observations invalidate the pooled estimates for the controlled studies in Dr. Davis meta-analysis, because they were weighted for the inverse of the variance in individual studies.

Second, turning to the 8 uncontrolled studies with 6-month data reported in Figure 3 of Dr. Davis' meta-analysis, 6 had very small sample size with follow-up data available in less than 20

patients (range, 8–20). Small studies with positive results are more readily reported than larger studies with negative results. Davis set a follow-up rate of less than 70% – not greater than 70% as stated in his paper – as the limit to determine high risk of bias. In fact the 6-month follow-up rate in 4 small studies with 10 up to 20 participants was 100%, but in all other studies it ranged from 53% to 66%. The pooled estimates of the 6-month BP responses in uncontrolled group were based on office BP in 6 studies and 24-h ambulatory monitoring in 2 studies (6,7). Results based on different techniques of BP measurement cannot be pooled in a single summary statistic. One wonders how a meta-analysis including only a single randomized trial of sufficient quality (3) adds to current knowledge. Dr. Davis concluded that RDN resulted in a substantial BP reduction at 6 months. In our view, this conclusion does not hold in view of the above issues. We believe that the main conclusion of Dr. Davis' meta-analysis should have been that currently the evidence in favor of RDN in treatment-resistant hypertension is of very low quality, that a meta-analysis cannot replace properly sized randomized clinical trials, and that RDN therefore should not be applied in routine clinical practice.

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